hypertension, and severe prostration during a mild infection suggested adrenal involvement, and investigations showed a 17-α-hydroxylase deficiency. Diagnosis of testicular feminization should not be made without excluding a defect of testosterone synthesis.

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Acute renal failure and gout as presenting features of acute lymphoblastic leukaemia

The 'preleukaemic' syndrome of pancytopenia and hypoplastic bone marrow has been described (Melhorn, Gross, and Newman, 1970). Hyperuricaemia (Sinks *et al.*, 1966), gout (Whitaker *et al.*, 1963), and uric acid nephropathy (Pochedly, 1973) are recognized complications of treating leukaemia. In our patient all these symptoms preceded the clinical onset of frank leukaemia. This has only been described once before (Appleyard, 1971). In this latter case renal failure was not the presenting feature but a later complication.

Case report

A 2½-year-old girl had been well until 6 months before admission. During this period she was fractious, developed polyuria and nocturia. Before admission her right foot and left wrist became painful, she vomited, became dehydrated, lethargic, and two bruises appeared. On admission she was pale, febrile, irritable, and dehydrated with Kussmaul respirations and hypotension. There was no lymphadenopathy, hepatosplenomegaly, renal enlargement, and the nervous system was normal. Her right foot, left ankle, left wrist, right third proximal interphalangeal joint were warm, swollen, and tender. She was oliguric. Her blood urea was 91 mmol/l (548 mg/100 ml), sodium 128 mmol/l (128 mEq/l), chloride 93 mmol/l (93 mEq/l), potassium 5·6 mmol/l (5·6 mEq/l), and bicarbonate 5 mmol/l (5 mEq/l). Treatment with intravenous saline and sodium bicarbonate corrected her dehydration and the renal failure improved without dialysis (Fig. 1). The joint symptoms resolved as the renal failure improved and the serum uric acid levels fell (Fig. 1).

Thrombocytopenia had been noted earlier, but within 4 days pancytopenia developed (Fig. 2). A bone marrow smear showed generalized hypocellularity with a relative increase in lymphoid and reticulum cells. There was no evidence of lymphoblastic change or malignancy. She was treated with blood transfusion and antibiotics and the pancytopenia gradually resolved (Fig. 2). The progress of the haematological and renal changes are shown in Figs. 1 and 2.

Other investigations were normal. Urine contained no crystals and was sterile. No viruses were isolated and blood cultures were sterile. *X*-rays showed no evidence of leukaemia and no abnormalities. Intravenous pyelogram on day 4 was normal. Renal biopsy on day 17 showed changes compatible with recovering tubular necrosis and two granulomata identical in appearance with those described in uric acid nephropathy.

She remained well until day 52 when she developed pains in several distal joints. She became restless, lethargic, vomited, and was readmitted on day 58 in acute renal failure (Fig. 1). She was reluctant to move either elbow, the left wrist, the proximal interphalangeal joints of the right 4th and 5th fingers and the left 5th toe. All were swollen and inflamed. Both kidneys were palpable and the liver was slightly enlarged. There was no splenomegaly, lymphadenopathy, or bruising. The acute renal failure and acidaemia were managed conservatively with dietary restriction and intravenous fluids (Fig. 1) and the serum uric acid levels fell.

Fig. 2 shows the results of blood tests at this time. The differential white cell count on day 60 showed immature red and white cells. Bone marrow examination on day 63 showed changes of acute undifferentiated leukaemia. On day 66 treatment was started with prednisolone 40 mg/m^2 per day and allopurinol; the

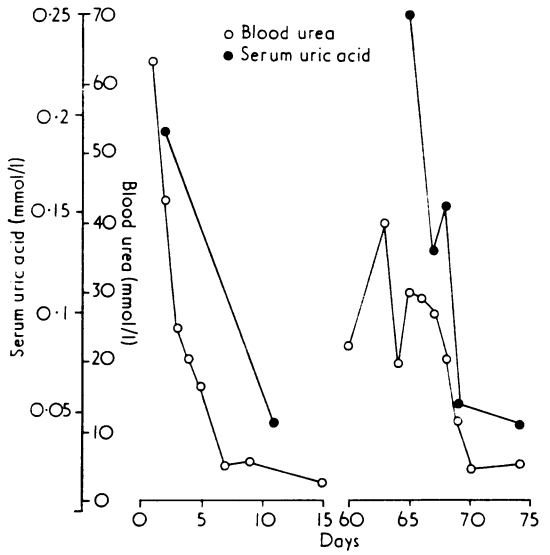

FIG. 1.—*Blood urea and serum uric acid levels during both admissions. Conversion: SI to traditional units—Blood urea: 1 mmol/l ≈ 6 mg/100 ml. Serum uric acid: 1 mmol/l ≈ 18 mg/100 ml.*

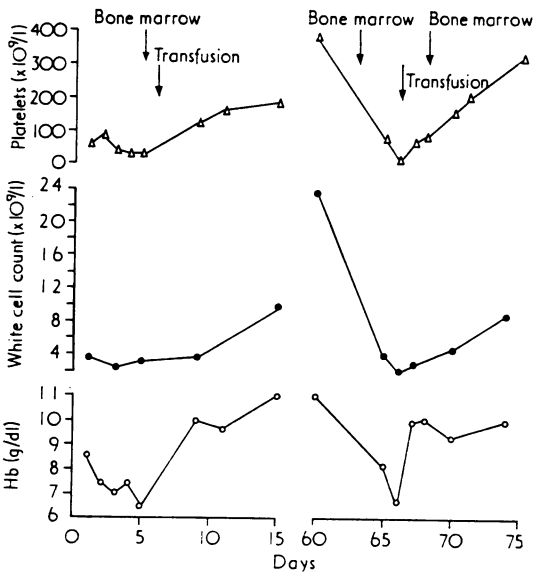

FIG. 2.—*Haemoglobin, white cell count, platelets, and bone marrows during both admissions. Conversion: SI to traditional units—Platelets: 150×10⁹/l ≈ 150 000/mm³. White cells: 1·0×10⁹/l ≈ 1000/mm³.*

following day the haemoglobin and platelet count had fallen and she was transfused (Fig. 2). Bone marrow examinations were repeated twice on day 67; both specimens (one obtained by trephine) were hypocellular. They were extensively studied but showed no evidence of leukaemia. Treatment continued with an injection of vincristine 1·5 mg/m² on day 73, and as her blood picture remained normal she was sent home on day 84 taking prednisolone and allopurinol. The arthropathy present on this admission had resolved by the time of discharge.

Follow-up. 3 weeks later treatment was changed to 6-mercaptopurine 40 mg/m² and the allopurinol was stopped. After one week uric acid had risen to 0·48 mmol/l (8·1 mg/100 ml), she developed discomfort in the left foot, and started limping so the allopurinol was restarted. After 2 days the uric acid level had fallen to 0·36 mmol/l (6·1 mg/100 ml) and the joint pains resolved. After this she was maintained on allopurinol and had no further episodes of renal failure or arthropathy. About 3 weeks later a transient facial palsy occurred, and a repeat bone marrow examination showed 10% blast cells. Examination of the cerebrospinal fluid showed 1200 blast cells/mm³. Her subsequent course has been stormy with haematological and central nervous system relapse, infections, and intestinal perforation. Her leukaemic treatment was unconventional. Vincristine was withheld initially to prevent further cell breakdown and worsening the renal failure. A single dose of vincristine was given on day 73. It was to be repeated in 3 weekly doses but the normal bone marrow at this time made us question the diagnosis and so she was continued on prednisolone. Generally, she has been very sensitive to antileukaemic agents and the doses have had to be small. Since relapse treatment has been with a variety of chemotherapeutic agents. She is still alive after 3 years. During all these complications the uric acid levels remained normal while allopurinol was given.

Discussion

It is most unusual to find acute renal failure along with arthropathy as the *presenting* feature of untreated childhood leukaemia and only one report is known to us (Appleyard, 1971). Even in this instance the renal failure occurred on the second admission. However, the pancytopenia and normal bone marrow are very reminiscent of this case.

The arthropathy and renal failure may not have been a direct result of hyperuricaemia but the close temporal relation strongly suggests a causal association. This was supported by finding uric acid granulomata in the renal medulla and a rapid mprovement in the arthritis as the uric acid level fell. The episodes of dehydration were probably also instrumental in producing renal damage. No leukaemic cells were found in the renal tissue. It is probable that during the first admission the leukaemia was remitting spontaneously (Diamond

and Luhby, 1951). However, it is possible that she may have had nonleukaemic marrow at one site and leukaemic marrow at another coincidentally. During the second admission the peripheral blood and bone marrow were briefly diagnostic of leukaemia. The patient's subsequent progress has left no doubt about the correctness of the diagnosis of acute undifferentiated leukaemia, later shown to be lymphoblastic by histochemistry and cytology of the bone marrow.

Summary

A leukaemic child is described who presented with renal failure and gout attributable to hyperuricaemia before the leukaemia could be diagnosed.

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